Practitioner's Docket No. 542-009-2

CHAPTER II

Preliminary Classification:

Proposed Class:

Subclass:

NOTE: "All applicants are requested to include a preliminary classification on newly filed patent applications. The preliminary classification, preferably class and subclass designations, should be identified in the upper right-hand corner of the letter of transmittal accompanying the application papers, for example 'Proposed Class 2, subclass 129.' " M.P.E.P., § 601, 7th ed.

TRANSMITTAL LETTER TO THE UNITED STATES ELECTED OFFICE (EO/US) (ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

PCT/JP99/05100 — INTERNATIONAL APPLICATION NO.

20 September 1999 — INTERNATIONAL FILING DATE

PRIORITY DATE CLAIMED

LIQUID PREPARATION FOR CONTACT LENSES

TITLE OF INVENTION

Kazuhiko NAKADA, Chikako NAKAMURA and Tatsuya HAYASHI

APPLICANT(S)

Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231
ATTENTION: EO/US

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10*
*(When using Express Mail, the Express Mail label number is **mandatory**; Express Mail certification is optional.)*

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☒ deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

37 C.F.R. § 1.8(a)

☐ with sufficient postage as first class mail.

37 C.F.R. § 1.10 *

☒ as "Express Mail Post Office to Addressee"
Mailing Label No. EV005526059US **(mandatory)**

TRANSMISSION

☐ facsimile transmitted to the Patent and Trademark Office, (703) _____-_____

Date: 3/20/02

Janet Gaffney
Signature

Janet Gaffney
(type or print name of person certifying)

** Only the date of filing (§ 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under § 1.8 continues to be taken into account in determining timeliness. See § 1.703(f). Consider "Express Mail Post Office to Addressee" (§ 1.10) or facsimile transmission (§ 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.*

NOTE: To avoid abandonment of the application, the applicant shall furnish to the USPTO, not later than 20 months from the priority date: (1) a copy of the international application, unless it has been previously communicated by the International Bureau or unless it was originally filed in the USPTO; and (2) the basic national fee (see 37 C.F.R. § 1.492(a)). The 30-month time limit may not be extended. 37 C.F.R. § 1.495.

WARNING: *Where the items are those which can be submitted to complete the entry of the international application into the national phase are subsequent to 30 months from the priority date the application is still considered to be in the international state and if mailing procedures are utilized to obtain a date the express mail procedure of 37 C.F.R. § 1.10 must be used (since international application papers are not covered by an ordinary certificate of mailing—See 37 C.F.R. § 1.8.*

NOTE: Documents and fees must be clearly identified as a submission to enter the national state under 35 U.S.C. § 371 otherwise the submission will be considered as being made under 35 U.S.C. § 111. 37 C.F.R. § 1.494(f).

I. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. § 371:

a. ☒ This express request to immediately begin national examination procedures (35 U.S.C. § 371(f)).

b. ☐ The U.S. National Fee (35 U.S.C. § 371(c)(1)) and other fees (37 C.F.R. § 1.492) as indicated below:

2. Fees

CLAIMS FEE	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
☐*	TOTAL CLAIMS	4 −20=		× $18.00=	$
	INDEPENDENT CLAIMS	1 −3=		× $84.00=	
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $280.00	
BASIC FEE**	☐ U.S. PTO WAS INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where an international preliminary examination fee as set forth in § 1.482 has been paid on the international application to the U.S. PTO: ☐ and the international preliminary examination report states that the criteria of novelty, inventive step (non-obviousness) and industrial activity, as defined in PCT Article 33(1) to (4) have been satisfied for all the claims presented in the application entering the national stage (37 C.F.R. § 1.492(a)(4)) ..... $100.00 ☐ and the above requirements are not met (37 C.F.R. § 1.492(a)(1)) ..... $710.00 ☐ U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in § 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in § 1.445(a)(2) to the U.S. PTO: ☐ has been paid (37 C.F.R. § 1.492(a)(2)) ..... $740.00 ☐ has not been paid (37 C.F.R. § 1.492(a)(3)) ..... $1040.00 ✗ ☒ where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 C.F.R. § 1.492(a)(5)) $890.00				$890.00
	Total of above Calculations				= $890.00
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable. Assertion must be made. (note 37 C.F.R. § 1.27)				−
	Subtotal				$890.00
	Total National Fee				$ 890.00
	Fee for recording the enclosed assignment document $40.00 (37 C.F.R. § 1.21(h)). (See Item 13 below). See attached "ASSIGNMENT COVER SHEET".				$40.00
TOTAL	Total Fees enclosed				$ 930.00

*See attached Preliminary Amendment Reducing the Number of Claims.

☒ Attached is a ☒ check ☐ money order in the amount of $ 930.00

☒ Authorization is hereby made to charge the amount of $ ~~for fee deficiency~~

☒ to Deposit Account No. 23-0442

☐ to Credit card as shown on the attached credit card information authorization form PTO-2038.

WARNING: *Credit card information should **not** be included on this form as it may become public.*

☐ Charge any additional fees required by this paper or credit any overpayment in the manner authorized above.

A duplicate of this paper is attached.

"WARNING: *"To avoid abandonment of the application the applicant shall furnish to the United States Patent and Trademark Office not later than the expiration of 30 months from the priority date: * * * (2) the basic national fee (see § 1.492(a)). The 30-month time limit may not be extended." 37 C.F.R. § 1.495(b).*

WARNING: *If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be met within a time period set by the Office. 37 C.F.R. § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40.*

☐ **Assertion of Small Entity Status**

☐ **Applicant hereby asserts status as a small entity under 37 C.F.R. § 1.27.**

NOTE: 37 C.F.R. § 1.27(c) deals with the assertion of small entity status, whether by a written specific declaration thereof or by payment as a small entity of the basic filing fee or the fee for the entry into the national phase as states:

"(c) Assertion of small entity status. Any party (person, small business concern or nonprofit organization) should make a determination, pursuant to paragraph (f) of this section, of entitlement to be accorded small entity status based on the definitions set forth in paragraph (a) of this section, and must, in order to establish small entity status for the purpose of paying small entity fees, actually make an assertion of entitlement to small entity status, in the manner set forth in paragraphs (c)(1) or (c)(3) of this section, in the application or patent in which such small entity fees are to be paid.

(1) Assertion by writing. Small entity status may be established by a written assertion of entitlement to small entity status. A written assertion must:

(i) Be clearly identifiable;

(ii) Be signed (see paragraph (c)(2) of this section); and

(iii) Convey the concept of entitlement to small entity status, such as by stating that applicant is a small entity, or that small entity status is entitled to be asserted for the application or patent. While no specific words or wording are required to assert small entity status, the intent to assert small entity status must be clearly indicated in order to comply with the assertion requirement.

(2) Parties who can sign and file the written assertion. The written assertion can be signed by:

(i) One of the parties identified in §§ 1.33(b) (e.g., an attorney or agent registered with the Office), §§ 3.73(b) of this chapter notwithstanding, who can also file the written assertion;

(ii) At least one of the individuals identified as an inventor (even though a §§ 1.63 executed oath or declaration has not been submitted), notwithstanding §§ 1.33(b)(4), who can also file the written assertion pursuant to the exception under §§ 1.33(b) of this part; or

(iii) An assignee of an undivided part interest, notwithstanding §§ 1.33(b)(3) and 3.73(b) of this chapter, but the partial assignee cannot file the assertion without resort to a party identified under §§ 1.33(b) of this part.

(3) Assertion by payment of the small entity basic filing or basic national fee. The payment, by any party, of the exact amount of one of the small entity basic filing fees set forth in §§ 1.16(a), (f), (g), (h), or (k), or one of the small entity basic national fees set forth in §§ 1.492(a)(1), (a)(2), (a)(3), (a)(4), or (a)(5), will be treated as a written assertion of entitlement to small entity status even if the type of basic filing or basic national fee is inadvertently selected in error.

(i) If the Office accords small entity status based on payment of a small entity basic filing or basic national fee under paragraph (c)(3) of this section that is not applicable to that application, any balance of the small entity fee that is applicable to that application will be due along with the appropriate surcharge set forth in §§ 1.16(e), or §§ 1.16(l).

(ii) The payment of any small entity fee other than those set forth in paragraph (c)(3) of this section (whether in the exact fee amount or not) will not be treated as a written assertion of entitlement to small entity status and will not be sufficient to establish small entity status in an application or a patent."

3. ☒ A copy of the International application as filed (35 U.S.C. § 371(c)(2)):

NOTE: *Section 1.495 (b) was amended to require that the basic national fee and a copy of the international application must be filed with the Office by 30 months from the priority date to avoid abandonment. "The International Bureau normally provides the copy of the international application to the Office in accordance with PCT Article 20. At the same time, the International Bureau notifies applicant of the communication to the Office. In accordance with PCT Rule 47.1, that notice shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place. Thus, if the applicant desires to enter the national stage, the applicant normally need only check to be sure the notice from the International Bureau has been received and then pay the basic national fee by 30 months from the priority date." Notice of Jan. 7, 1993, 1147 O.G. 29 to 40, at 35-36. See item 14c below.*

a. ☒ is transmitted herewith.

b. ☐ is not required, as the application was filed with the United States Receiving Office.

c. ☐ has been transmitted

i. ☐ by the International Bureau.

Date of mailing of the application (from form PCT/1B/308):

_____.

ii. ☐ by applicant on _____. *(Date)*

4. ☒ A translation of the International application into the English language (35 U.S.C. § 371(c)(2)):

a. ☒ is transmitted herewith.

b. ☐ is not required as the application was filed in English.

c. ☐ was previously transmitted by applicant on _____. *(Date)*

d. ☐ will follow.

5. ☐ Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. § 371(c)(3)):

NOTE: The Notice of January 7, 1993 points out that 37 C.F.R. § 1.495(a) was amended to clarify the existing and continuing practice that PCT Article 19 amendments must be submitted by 30 months from the priority date and this deadline may not be extended. The Notice further advises that: "The failure to do so will not result in loss of the subject matter of the PCT Article 19 amendments. Applicant may submit that subject matter in a preliminary amendment filed under section 1.121. In many cases, filing an amendment under section 1.121 is preferable since grammatical or idiomatic errors may be corrected." 1147 O.G. 29-40, at 36.

a. ☐ are transmitted herewith.

b. ☐ have been transmitted

i. ☐ by the International Bureau.

Date of mailing of the amendment (from form PCT/1B/308):

_____.

ii. ☐ by applicant on _____. *(Date)*

c. ☐ have not been transmitted as

i. ☐ applicant chose not to make amendments under PCT Article 19. Date of mailing of Search Report (from form PCT/ISA/210.):

_____.

ii. ☐ the time limit for the submission of amendments has not yet expired. The amendments or a statement that amendments have not been made will be transmitted before the expiration of the time limit under PCT Rule 46.1.

6. ☐ A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. § 371(c)(3)):

a. ☐ is transmitted herewith.

b. ☐ is not required as the amendments were made in the English language.

c. ☐ has not been transmitted for reasons indicated at point 5(c) above.

7. ☒ A copy of the international examination report (PCT/IPEA/409)

☒ is transmitted herewith.

☐ is not required as the application was filed with the United States Receiving Office.

8. ☐ Annex(es) to the international preliminary examination report

a. ☐ is/are transmitted herewith.

b. ☐ is/are not required as the application was filed with the United States Receiving Office.

9. ☐ A translation of the annexes to the international preliminary examination report

a. ☐ is transmitted herewith.

b. ☐ is not required as the annexes are in the English language.

10. ☒ An oath or declaration of the inventor (35 U.S.C. § 371(c)(4)) complying with 35 U.S.C. § 115

a. ☐ was previously submitted by applicant on _____. *(Date)*

b. ☒ is submitted herewith, and such oath or declaration

i. ☒ is attached to the application.

ii. ☐ identifies the application and any amendments under PCT Article 19 that were transmitted as stated in points 3(b) or 3(c) and 5(b); and states that they were reviewed by the inventor as required by 37 C.F.R. § 1.70.

c. ☐ will follow.

II. Other document(s) or information included:

11. ☒ An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a):

a. ☒ is transmitted herewith.

b. ☐ has been transmitted by the International Bureau.

Date of mailing (from form PCT/IB/308): _____.

c. ☐ is not required, as the application was searched by the United States International Searching Authority.

d. ☐ will be transmitted promptly upon request.

e. ☐ has been submitted by applicant on _____. *(Date)*

12. ☒ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98:

a. ☒ is transmitted herewith.

Also transmitted herewith is/are:

☒ Form PTO-1449 (PTO/SB/08A and 08B).

☒ Copies of citations listed.

b. ☐ will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. § 371(c).

c. ☐ was previously submitted by applicant on _____. *(Date)*

13. ☒ An assignment document is transmitted herewith for recording.

A separate ☒ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

_____

_____

_____

14. ☒ Additional documents:

a. ☐ Copy of request (PCT/RO/101)

b. ☒ International Publication No. WO 01/20997 A1

i. ☐ Specification, claims and drawing

ii. ☒ Front page only

c. ☐ Preliminary amendment (37 C.F.R. § 1.121)

d. ☐ Other

15. ☒ The above checked items are being transmitted

a. ☒ before 30 months from any claimed priority date.

b. ☐ after 30 months.

16. ☐ Certain requirements under 35 U.S.C. § 371 were previously submitted by the applicant on _____, namely:

AUTHORIZATION TO CHARGE ADDITIONAL FEES

WARNING: *Accurately count claims, especially multiple dependant claims, to avoid unexpected high charges if extra claims are authorized.*

NOTE: "A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission." 37 C.F.R. § 1.136(a)(3).

NOTE: "Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account." 37 C.F.R. § 1.26(a).

☐ Please charge, in the manner authorized above, the following additional fees that may be required by this paper and during the entire pendency of this application:

☐ 37 C.F.R. § 1.492(a)(1), (2), (3), and (4) (filing fees)

WARNING: *Because failure to pay the national fee within 30 months without extension (37 C.F.R. § 1.495(b)(2)) results in abandonment of the application, it would be best to always check the above box.*

☐ 37 C.F.R. § 1.492(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 C.F.R. § 1.492(d)), it might be best not to authorize the PTO to charge additional claim fees, except possible when dealing with amendments after final action.

☐ 37 C.F.R. § 1.17 (application processing fees)

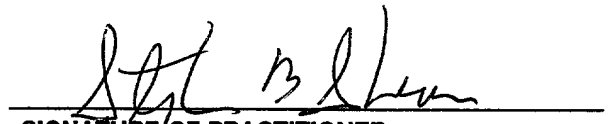
☐ 37 C.F.R. § 1.17(a)(1)–(5) (extension fees pursuant to § 1.136(a).

☐ 37 C.F.R. § 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. § 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 C.F.R. § 1.311(b).

NOTE: 37 C.F.R. § 1.28(b) requires "Notification of any change in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying . . . issue fee." From the wording of 37 C.F.R. § 1.28(b): (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

☐ 37 C.F.R. § 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 30 months after the priority date).



SIGNATURE OF PRACTITIONER

Stephen B. Shear

(type or print name of practitioner)

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Customer No.: 004955

PATENT
Attorney Docket
542-009-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Nakada et al.

Serial No.: To be assigned

Filed: herewith

Title: LIQUID PREPARATION FOR CONTACT LENSES

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

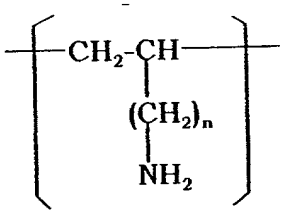
Kindly enter the following Amendment and Remarks in this application before examination.

PRELIMINARY AMENDMENT

In the claims:

Please amend claims 1 through 4 as follows:

1. A liquid preparation for use in conjunction with contact lenses comprising 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



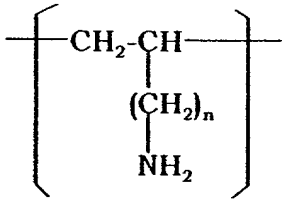
(I)

wherein n is 0 or 1.

2. The liquid preparation of Claim 1, further comprising at least one member selected from the group consisting of an antiseptic agent, a chelating agent, a buffer, an isotonizing agent, a thickener, a surface active agent and an antibacterial assistant.

3. The liquid preparation of Claim 2, wherein the surface active agent is a member selected from the group consisting of a nonionic surface active agent, a cationic surface agent and an ampholytic surface active agent.

4. A process for preserving, cleaning or disinfecting contact lenses comprising contacting said lenses with a liquid preparation comprising 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):

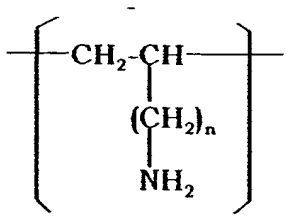


(I)

wherein n is 0 or 1.

Please add claim 5 as follows:

5. A process for shipping contact lenses comprising shipping said lenses in a solution comprising 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



(I)

wherein n is 0 or 1.

REMARKS

The above amendments to the claims are made for the purpose of putting the claims into a form which complies with requirements of U.S. practice, and to facilitate examination. The amendment is in order and its entry is earnestly solicited.

Attorney Docket 542-009-2

A "Version With Markings to Show Changes Made" is attached with respect to the amendments to the claims made above.

Respectfully submitted,

Date: March 20, 2002

By Stephen B. Shear
Stephen B. Shear
Registration No. 28,116
Attorney for Applicant

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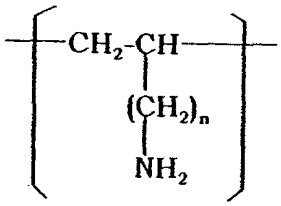
Customer No. 004955

Version With Markings to Show Changes Made

In the claims:

1. (Amended) A liquid preparation for use in conjunction with contact lenses [containing] comprising 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



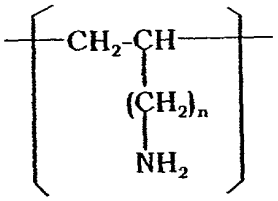
(I)

wherein n is 0 or 1.

2. (Amended) The liquid preparation of Claim 1, [which contains] further comprising at least one member selected from the group consisting of an antiseptic agent, a chelating agent, a buffer, an isotonizing agent, a thickener, a surface active agent and an antibacterial assistant.

3. (Amended) The liquid preparation of Claim [1]2, [which is used as a shipping solution, a preserving solution, a cleaning solution or a disinfecting solution, or for at least two purposes selected from preservation, cleaning and disinfection] wherein the surface active agent is a member selected from the group consisting of a nonionic surface active agent, a cationic surface agent and an ampholytic surface active agent.

4. (Amended) [The liquid preparation of Claim 1, wherein the surface active agent is a member selected from the group consisting of a nonionic surface active agent, a cationic surface active agent and an ampholytic surface active agent.] A process for preserving, cleaning or disinfecting contact lenses comprising contacting said lenses with a liquid preparation comprising 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):

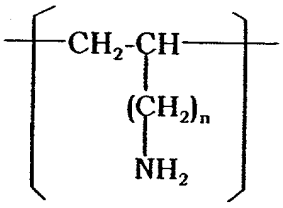


(I)

wherein n is 0 or 1.

Please add the following new claim 5.

5. A process for shipping contact lenses comprising shipping said lenses in a solution comprising 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



(I)

wherein n is 0 or 1.

DESCRIPTION

LIQUID PREPARATION FOR CONTACT LENSES

TECHNICAL FIELD

The present invention relates to a liquid preparation for contact lenses, and more particularly to a liquid preparation for contact lenses which can be suitably used, for example, for cleaning, preserving, disinfecting or rinsing contact lenses.

BACKGROUND ART

Contact lenses are required to conduct cleaning treatment since soils such as proteins and lipids derived from lachrymal tears may adhere to the lenses. In order to prevent contamination by microorganisms such as bacteria and fungi during preservation of contact lenses, it is also required to disinfect contact lenses taken off from the eyes and to preserve them in an appropriate solution until they are worn again. Such treatments for cleaning, disinfection and preservation are unavoidable in safely wearing contact lenses.

However, procedures for cleaning, disinfecting and preserving contact lenses are very complicated. Moreover, several kinds of liquid preparations such as cleaning solution, disinfecting solution and preserving solution must be provided against these treatments. Trouble and cost required for use and maintenance of contact lenses impose a large burden on the users.

Thus, as one capable of solving such problems, multi-purpose liquid preparations for contact lenses that treatments (cleaning,

rinsing, disinfecting and preservation) necessary for the maintenance of contact lenses can be made with the use of a single liquid preparation, are put on the market at present here and abroad. That is to say, these liquid preparations comprises a preserving solution to which surfactant, antibacterial agent and the like are added so that all of cleaning treatment, rinsing treatment, disinfecting treatment and preservation can be made by such a single liquid preparation.

With respect to this type of the liquid preparations for contact lenses, various compounds have been heretofore investigated as antibacterial agents to be added thereto. However, these compounds all must be used in a high concentration for obtaining a practical high antibacterial activity. The use on such a high level of concentration may raise a problem in safety since toxicity is strong and there is the danger of giving irritation to mucous membrane of the eyes to cause inflammation. Thus, investigation has been made so that a higher antibacterial effect can be obtained by the use of a smaller amount of antibacterial agent.

For example, in JP-A-6-321715, it is proposed to use a biguanide derivative in combination with a borate buffer to provide a disinfecting and preserving solution which has a low toxicity to the eyes while having a high level of antibacterial activity. In JP-A-6-504044, it is also proposed to use a biguanide derivative in combination with a tris buffer to provide a disinfecting composition for contact lenses which has substantially no irritation while having an excellent disinfecting property. However, the antibacterial effect of these liquid preparations for contact lenses is still insufficient.

Accordingly, it is an object of the present invention to provide

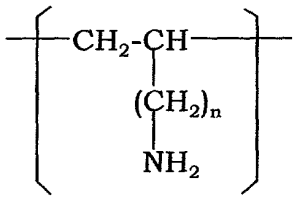
a liquid preparation for contact lenses which can exhibit an excellent antibacterial effect or antiseptic effect while securing a high safety to the eyes.

A further object of the present invention is to provide a liquid preparation for contact lenses which enables to wear the disinfected contact lenses directly on the eyes without rinsing them with another rinsing solution.

DISCLOSURE OF INVENTION

The present inventors have found, as a result of making an intensive study to solve the above-mentioned problems, that when a specific polyamine is used as an antibacterial component, a sufficient disinfecting effect is exhibited even if it is used in a lower concentration than conventional level.

Thus, in accordance with the present invention, there is provided a liquid preparation for contact lenses containing 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



(I)

wherein n is 0 or 1.

The liquid preparation for contact lenses of the present invention is suitable for use as a shipping solution, a preserving solution, a cleaning solution and a disinfecting solution, or for use in a combination of at least two of preservation, cleaning and disinfection.

Since the polyamine which is used herein as an antibacterial agent has a high antibacterial activity and the concentration of the

antibacterial agent which is necessary to exhibit the same level of the antibacterial or antiseptic effect as that of conventional disinfecting solutions for contact lenses, can be held low, the liquid preparation of the present invention can advantageously decrease the amount of the antibacterial agent and, therefore, the safety to the eyes can be further raised.

BEST MODE FOR CARRYING OUT THE INVENTION

In accordance with a preferable embodiment of the liquid preparation for contact lenses of the present invention, a higher safety to the eyes can be secured by using an aqueous medium as a medium and by adjusting the liquid preparation to a pH of 5 to 8 and an osmotic pressure of 250 to 350 mOsm/kg.

Also, in such a liquid preparation of the present invention, advantageously a polyhydric alcohol is used in order to enhance the antibacterial activity of the polyamine. The concentration thereof is from 0.1 to 3 w/v %. As such a polyhydric alcohol are preferably used dihydric and trihydric alcohols having a main chain composed of an alkylene group having 2 to 8 carbon atoms. Of these, the use of those having a main chain composed of an alkylene group having 2 to 5 carbon atoms is particularly advantageous in enhancing the antibacterial effect. When it is desired to prevent contact lenses from swelling, those having a main chain composed of an alkylene group having 4 to 8 carbon atoms are advantageously used.

Besides, in such a liquid preparation of the present invention, the polyamine is included in the aqueous medium in a concentration of 0.3 to 50 ppm. The polyamine may be used in combination with at least

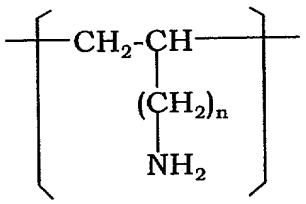
one other organic nitrogen-containing antibacterial agent selected as an antibacterial assistant or an antiseptic agent from the group consisting of a quaternary ammonium compound or its polymer, a biguanide compound or its polymer, a copolymer of the quaternary ammonium compound and the biguanide compound, and an ampholytic surface active agent. These antibacterial assistants or antiseptic agents are added to the liquid preparation for contact lenses, for example, in an amount of 0.1 to 1 ppm, provided that it is preferable that the amount thereof is not more than the amount of the polyamine.

In another preferable embodiment of the present invention, the liquid preparation for contact lenses further contains at least one member selected from the group consisting of a non-ionic surface active agent, a non-ionic or cationic thickening agent, a buffer and a chelating agent. Desired effects are imparted to the liquid preparation by the incorporation of these components. For example, a cleaning effect is imparted to the liquid preparation by the incorporation of a non-ionic surface active agent. An adequate viscosity and slippage are imparted by the incorporation of a non-ionic or cationic thickening agent, whereby can be achieved the effects that it becomes easier to clean contact lenses, soils are prevented from adhering to contact lenses again, a hydrophilic property is imparted to contact lenses, and in case that rinsing is not needed, the feel of wearing contact lenses on the eyes becomes better. The incorporation of a buffer has the advantage that the pH of the preparation liquid is stabilized, whereby irritation and disorder to the eyes can be avoided. The incorporation of a chelating agent has the advantage that a chelating effect is imparted to contact lenses, whereby the lenses can be protected from bad influences exerted by metal ions.

Preferable examples of the buffer are hydroxyalkylamines and their derivatives. Of these, bis(2-hydroxyethyl)iminotris(hydroxymethyl)-methane is particularly preferred since it has an excellent effect of removing lachrymal soils. As the thickening agent are preferably used saccharide derivatives, particularly cellulose derivatives, since there is no danger of exerting a bad influence on the physical properties of lens even in preservation for a long term.

As mentioned above, in one of preferable embodiments of the present invention, a specific amount of a polyhydric alcohol is included in a medium composed mainly of water together with a polyamine, whereby a synergistic antibacterial or antiseptic effect is exhibited. Thus, by utilizing such a synergistic antibacterial or antiseptic effect, there is provided a useful liquid preparation for contact lenses that enables to conduct the disinfecting treatment of contact lenses more simply and easily and to directly wear the treated contact lenses.

The polyamines used in the present invention are polymers having recurring units of the formula (I):



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wherein n is 0 or 1. The polyamines may be homopolymers or copolymers with other radically copolymerizable monomers, particularly a hydrophilic vinyl monomer. The content of the other radically copolymerizable monomers is preferably not more than 50 % by weight, more preferably not more than 30 % by weight. Examples of the other radically copolymerizable monomers are, for instance, a hydroxyalkyl (meth)acrylate such as hydroxymethyl (meth)acrylate, hydroxypropyl

(meth)acrylate or hydroxybutyl (meth)acrylate, N-vinylpyrolidone, (meth)acrylamide, dimethyl (meth)acrylamide, and the like. Polyallylamine is prepared by polymerizing allylamine in a known manner. Polyvinylamines are prepared from vinylamine derivatives in a known manner.

From the viewpoint that certain degree of molecular weight is needed for sufficiently obtaining the antiseptic effect and the antibacterial effect, it is desirable that the weight average molecular weight of the polyamine is not less than about 500, preferably not less than about 1,000. Also, from the viewpoints that lowering of solubility in the medium such as water may make it difficult to obtain a uniform liquid preparation and increase in viscosity may raise a problem in handling, it is desirable that the weight average molecular weight of the polyamine is not more than about 200,000, preferably not more than about 100,000.

The content of the polyamine in the liquid preparation for contact lenses is preferably not less than 0.3 ppm from the viewpoint of sufficiently exhibiting the antiseptic and antibacterial effects of the polyamine, and is preferably not more than 50 ppm from the viewpoint of safety.

Examples of the quaternary ammonium compounds (including those in the form of salt) or their polymers which are used in the present invention as an antibacterial assistant or an antiseptic agent are, besides known cationic surface active agents, polycations such as condensates of diamines and dihalogen compounds as disclosed in Japanese Patent No. 2,550,036, benzalkonium halides, and the like. Any of them can be used so long as they are ophthalmologically

acceptable.

Representative cationic surface active agents are alkylammonium salts, and as the alkylammonium salts can be used tetraalkylammonium salts. Examples of the tetraalkylammonium salts are, for instance, an alkyltrimethylammonium chloride such as octadecyltrimethylammonium chloride, dioleyldimethylammonium chloride, dodecyltrimethylammonium chloride, didecyldimethylammonium chloride, acylalkyltrimethylammonium chloride, tetradecyltrimethylammonium chloride or hexadecyltrimethylammonium chloride, octadecyltrimethylammonium bromide, dioleyldimethylammonium bromide, dodecyltrimethylammonium bromide, didecyldimethylammonium bromide, acylalkyltrimethylammonium bromide, tetradecyltrimethylammonium bromide, hexadecyltrimethylammonium bromide, and the like. Trialkylbenzylammonium bromides can also be used, e.g., octadecyldimethylbenzylammonium chloride and octadecyldimethylbenzylammonium bromide. Further, other ophthalmologically acceptable cationic surface active agents can also be used without any restriction, e.g., alkylhydroxyalkylimidazoline quaternary salts as represented by hydroxyethylalkylimidazolinium chloride, alkylisoquinolinium salts as represented by alkylisoquinolinium bromide, alkylpyridinium salts, and amidoamines.

Representative ampholytic surface active agents which are used as an antibacterial assistant or an antiseptic agent are, for instance, alkylglycines. Examples of the alkylglycines are an alkylaminoethylglycine hydrochloride such as dodecyl(aminoethyl)glycine hydrochloride; an alkyldi(aminoethyl)glycine hydrochloride such as tetradodecyldi(aminoethyl)glycine hydrochloride

or lauryldi(aminoethyl)glycine hydrochloride; an alkylpoly(aminoethyl)-glycine hydrochloride such as octylpoly(aminoethyl)glycine hydrochloride; dodecylguanidine hydrochloride; di(octylaminoethyl)-glycine hydrochloride; and the like. Any of other ampholytic surface active agents can also be used so long as they are ophthalmologically acceptable, e.g., alkylbetaines such as dimethylalkylbetaine, imidazolines such as alkylimidazoline, amidobetaines, acyl-hydrolyzed collagen peptide salt, and betain acetate.

As the biguanide compounds or their polymers can be used known biguanide antibacterial agents such as polyhexamethylene biguanide.

The polyhydric alcohol which is used together with the polyamine in the present invention serves to enhance the antibacterial activity of the polyamine. Since the antiseptic effect and the disinfecting effect of the liquid preparation for contact lenses can be remarkably improved by the combination use of them, the liquid preparation can exhibit effective antibacterial or disinfecting effects even if the amount of the polyamine is decreased.

The polyhydric alcohol is an alcohol having at least two hydroxyl groups, and ophthalmologically acceptable ones are suitably selected from known polyhydric alcohols. Of these, preferable are a dihydric alcohol such as an alkylene glycol or derivatives thereof, and a dihydric or trihydric alcohol such as glycerol or derivatives thereof. In particular, dihydric and trihydric alcohols having a main chain composed of an alkylene group having 2 to 8 carbon atoms, especially dihydric and trihydric alcohols having a main chain composed of a saturated alkylene group having 2 to 5 carbon atoms, are preferably

used from the viewpoint of enhancement of antibacterial effect, e.g., ethylene glycol, propylene glycol, butylene glycol and pentylene glycol. When it is desired to prevent contact lenses from swelling, it is preferable to use dihydric and trihydric alcohols having a main chain composed of a saturated alkylene group having 4 to 8 carbon atoms, e.g., butylene glycol, pentylene glycol and hexylene glycol. The amount of the polyhydric alcohol is from 0.01 to 5 w/v %, preferably 0.1 to 3 w/v %, more preferably 0.5 to 2.5 w/v %, based on the liquid preparation for contact lenses. If the amount of the polyhydric alcohol is too small, the effect of enhancing the antibacterial activity produced by the use thereof is not sufficiently achieved. If the amount is more than 5 w/v %, the osmotic pressure of the liquid preparation itself increases to cause stimulation to the eyes and, in addition, problems arise particularly on soft contact lenses, such as change in lens size, deterioration of the feel of wear caused by change in fitting, occurrence of visual impairment and stimulation to the eyes.

It is preferable that the liquid preparation for contact lenses of the present invention is adjusted to a pH of 5 to 8, especially a pH in the vicinity of 7.0, and to an osmotic pressure of 250 to 350 mOsm/kg. If the pH and osmotic pressure are outside the above ranges, there is a possibility of giving stimulation to the eyes or causing disorder. Preferable pH adjusting agents used for such pH adjustment are sodium hydroxide and potassium hydroxide. Isotonizing agents used for adjusting the osmotic pressure include ophthalmologically acceptable inorganic salts, typically sodium chloride and potassium chloride.

In order to effectively keep the pH of the liquid preparation for contact lenses within the above-mentioned range and within the range

safe for the eyes, at least one buffer is usually added. The buffer is suitably selected from various kinds of conventionally known buffers. Examples of the buffers which, in particular, are safe for the eyes and have less influence on contact lenses, are acids, e.g., citric acid, malic acid, lactic acid, ascorbic acid, maleic acid, gluconic acid, phosphoric acid, boric acid, an hydroxy carboxylic acid, an amino acid such as glycine or glutamic acid, and tris(hydroxymethyl)aminomethane (Tris); their salts (e.g., sodium salts); Good-Buffer containing taurine or its derivatives; a hydroxyalkylamine such as bis(2-hydroxyethyl)imino-tris(hydroxymethyl)methane (Bis-tris); and the like. Of these, citric acid and its salts, phosphoric acid, boric acid, Good-Buffer and hydroxyalkylamines are preferred. In particular, hydroxyalkylamines, especially Bis-tris, are preferably used from the viewpoint of effectively removing lachrymal soils. The amount of the buffer is usually from about 0.01 to about 2 w/v % based on the liquid preparation for contact lenses. If the concentration of the buffer is too low, a desired buffering effect is not sufficiently exhibited. Also, even if the buffer is used in a higher amount, the pH stability is not necessarily further improved and, rather, there is a possibility of exerting a bad influence on safety such as stimulation to the eyes resulting from increase in osmotic pressure.

Preferably the liquid preparation for contact lenses of the present invention is incorporated with a non-ionic surface active agent in order to effectively exhibit the effect of removing soils such as lipids adhering to contact lenses. The use of anionic surface active agents is not desirable since there is a danger of reacting with the polyamine used in the present invention to result in production of a precipitate.

Any of known non-ionic surface active agents can be used so

long as they have a high safety to the living body and have no influence on contact lens materials. Examples of the non-ionic surface active agents are a polyglyceryl fatty acid ester, a polyoxyethylene alkyl ether, a polyoxyethylene-polyoxypropylene block copolymer, a polyoxyethylene-polyoxypropylene ethylenediamine, a polyoxyethylene alkylphenyl ether formaldehyde condensate, a polyoxyethylene hydrogenated castor oil, a polyoxyethylene alkylphenyl ether, a polyoxyethylene glycerol fatty acid ester, a polyoxyethylene sorbitan fatty acid ester, a polyoxyethylene castor oil, a polyoxyethylene sterol ether, a polyoxyethylene hydrogenated sterol ether, a polyoxyethylene fatty acid ester, a polyoxyethylene-polyoxypropylene alkyl ether, a polyoxyethylene lanolin alcohol, a polyoxyethylene alkylamine, a polyoxyethylene alkylamide, a polyoxyethylene alkyl ether phosphate, a polysorbate, and the like.

Of these, preferable are a polyoxyethylene alkyl ether such as polyoxyethylene lauryl ether, a polyoxyethylene-polyoxypropylene block copolymer of Pulronic type or Tetronic type, a polyoxyethylene sorbitan fatty acid ester, a polyoxyethylene alkylphenyl ether formaldehyde condensate such as Thiloxapol, a polyoxyethylene hydrogenated castor oil, a polyoxyethylene alkylphenyl ether, a polyoxyethylene fatty acid ester such as polyoxyethylene stearate, and a polysorbate.

The amount of the non-ionic surface active agent is generally from about 0.001 to about 5 w/v %, preferably from about 0.005 to about 2 w/v %, more preferably from about 0.01 to about 1 w/v %, based on the liquid preparation for contact lenses. If the amount is less than 0.001 w/v %, the cleaning effect is insufficient. Even if the amount is more than 5 w/v %, no increase in cleaning effect is obtained and it may rather stimulate the eyes.

The liquid preparation for contact lenses of the present invention may be incorporated with a thickener as occasion demands. Non-ionic or cationic thickeners can be used, e.g., various gums such as heteropolysaccharides, synthetic organic polymers such as polyvinyl alcohol, poly-N-vinylpyrrolidone, polyethylene glycol, polypropylene glycol and polyacrylamide, cellulose derivatives, and starch derivatives. Such thickeners are advantageously used from the viewpoints that slippability between fingers and contact lens at the time of cleaning the contact lens with the fingers becomes better and, consequently, the cleaning property is improved. Of these, saccharide derivatives, especially cellulose derivatives, are preferably used from the viewpoint that there is no danger of exerting a bad influence on the physical properties of lens even in the preservation for a long term. Examples of such cellulose derivatives are, for instance, methyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose and the like.

The liquid preparation for contact lenses of the present invention may also contain other additives such as a chelating agent. Any of conventionally known additives can be used so long as they are safe for the living body and have no influence on contact lens materials, and can be incorporated into the contact lens liquid preparation as occasion demands.

In particular, it is preferable to incorporate a metal chelate-forming agent into the contact lens liquid preparation of the present invention in order to prevent a metal ion such as calcium ion in the tears from being adsorbed by contact lenses, especially soft contact lenses. Examples of such a chelating agent are ethylenediaminetetraacetic acid

(EDTA) and its salts such as disodium ethylenediaminetetraacetate (EDTA·2Na) and trisodium ethylenediaminetetraacetate (EDTA·3Na); citric acid, gluconic acid, tartaric acid and their salts, e.g., sodium salts. In particular, EDTA, EDTA·2Na and EDTA·3Na are preferred. The amount of the chelating agent is generally from about 0.01 to about 2 w/v % based on the liquid preparation for contact lenses. If the amount of the chelating agent is small, a sufficient effect is not expected. Even if the amount is large, the effect of the chelating agent does not further increase.

The contact lens care with the liquid preparation of the present invention is conducted in the following manner. For example, contact lenses taken off from the eyes are rubbed with the liquid preparation of the present invention, rinsed with the liquid preparation, and then immersed in the liquid preparation for a predetermined time, generally at least 30 minutes, preferably at least 2 hours, usually overnight, in a suitable container filled with the liquid preparation, thereby achieving the preservation and disinfection of the contact lenses. When the contact lenses are worn again, the lenses are taken out of the liquid preparation and worn on the eyes. Since the liquid preparation of the present invention is safe to the eyes, it is not required to rinse the lenses with physiological saline or the like and, therefore, the lenses immersed in the liquid preparation are taken out and can be directly worn on the eyes. That is to say, if the liquid preparation for contact lenses of the present invention is used, the contact lens care can be very simply and easily carried out since all of cleaning, preservation, disinfection and rinsing of contact lenses can be achieved by only the liquid preparation.

All kinds of contact lenses can be treated with the liquid preparation of the present invention without any restriction. For example, the liquid preparation of the present invention is applicable to all kinds of soft contact lenses such as low water-containing type and high water-containing type, and hard contact lenses, and the materials of the contact lenses and the like are not restricted upon the application of the liquid preparation.

The present invention is then specifically explained by means of Examples, but it is to be understood that the present invention is not limited to these Examples.

EXAMPLES 1 AND 2 AND COMPARATIVE EXAMPLES 1 TO 3

A liquid preparation for contact lenses was prepared by dissolving polyallylamine having a weight average molecular weight of about 10,000 in water in a concentration shown in Table 1. The disinfecting test of the obtained liquid preparation was made in the following manner.

(A) Disinfecting test

The disinfecting test and evaluation of the liquid preparation were made according to United States Pharmacopoeia 23 using Candida albicans IFO 1594 and Pseudomonas aeruginosa IFO 13275 as test microorganisms. The results are shown in Table 1, wherein the values denote Log reduction of the number of viable cells of the microorganism which were inoculated and allowed to stand at room temperature for 4 hours.

COMPARATIVE EXAMPLE 4

The procedure of Example 1 was repeated except that 1 ppm of polyhexamethylene biguanide (PHMB) was used as an antibacterial agent instead of polyallylamine. The result is shown in Table 1.

Table 1

	Concentration of polyallylamine (w/v %)	Log reduction	
		P. aeruginosa	C. albicans
Com. Ex. 1	0.12 (=1,200 ppm)	>3.04	4.16
Com. Ex. 2	0.012 (=120 ppm)	>3.04	3.86
Example 1	0.0012 (=12 ppm)	>3.57	>3.87
Example 2	0.00012 (=1.2 ppm)	>3.57	1.18
Com. Ex. 3	0.000012 (=0.12 ppm)	-0.95	-0.04
Com. Ex. 4	PHMB (1 ppm)	-	0.46

(Note) PHMB: polyhexamethylene biguanide

As shown in Table 1, the concentrations of bactericidal agent in the liquid preparations of Example 1 and Comparative Example 2 are different from each other by 10 times, but the bactericidal effects thereof to P. aeruginosa and C. albicans are on the same level. Also, in case of using 1 ppm of polyhexamethylene biguanide (PHMB) which has been conventionally used as a bactericidal agent (Comparative Example 4), no sufficient bactericidal effect is obtained since the value to C. albicans is low. Further, if the polyamine concentration is too low (Comparative Example 3), no sufficient bactericidal effect is obtained since the values to P. aeruginosa and C. albicans are low.

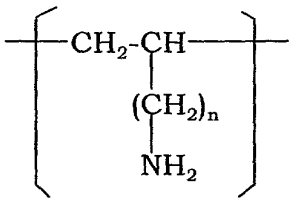
INDUSTRIAL APPLICABILITY

The liquid preparation for contact lenses of the present

invention has an excellent antibacterial or antiseptic effect, and can be advantageously used for the purpose of every treatment of contact lenses such as cleaning, preservation, disinfection and rinsing.

CLAIMS

1. A liquid preparation for contact lenses containing 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



(I)

wherein n is 0 or 1.

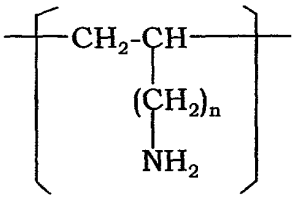
2. The liquid preparation of Claim 1, which contains at least one member selected from the group consisting of an antiseptic agent, a chelating agent, a buffer, an isotonizing agent, a thickener, a surface active agent and an antibacterial assistant.

3. The liquid preparation of Claim 1, which is used as a shipping solution, a preserving solution, a cleaning solution or a disinfecting solution, or for at least two purposes selected from preservation, cleaning and disinfection.

4. The liquid preparation of Claim 1, wherein the surface active agent is a member selected from the group consisting of a non-ionic surface active agent, a cationic surface active agent and an ampholytic surface active agent.

ABSTRACT

A highly safe liquid preparation for contact lenses which contains 0.3 to 50 ppm of a polyamine having recurring units of the formula (I):



(I)

wherein n is 0 or 1, and which has a high antibacterial effect even at low concentrations.

COMBINED DECLARATION AND POWER OF ATTORNEY

(Docket Number)

As a below named inventor, I hereby declare that:

- my residence, post office address and citizenship are as stated below next to my name;
- I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **LIQUID PREPARATION FOR CONTACT LENSES,**
- the specification of which is attached hereto unless the following box is checked: ☒. If the box is checked,

  the application was filed on **September 20, 1999**
  as U.S. Application Number
  or PCT International Application Number **PCT/JP99/05100**
  and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application			Priority Not Claimed
(Application Number)	(Country)	(Day/Month/Year Filed)	☐
(Application Number)	(Country)	(Day/Month/Year Filed)	☐

To the extent permitted by rule or law, I hereby incorporate by reference the Prior Foreign Application(s) listed above.

I hereby claim the benefits under 35 U.S.C. §119(e) of any United States provisional application(s) listed below:

(Provisional Application Number)	(Day/Month/Year Filed)
(Provisional Application Number)	(Day/Month/Year Filed)

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s), or §365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose information which is material to patentability, as defined in 37 CFR §1.56, which became available between the filing date of the prior application and the national or PCT International filing date of this application.

(Application Number)	(Day/Month/Year Filed)	(Status--patented, pending, abandoned)
(Application Number)	(Day/Month/Year Filed)	(Status--patented, pending, abandoned)

I hereby appoint the attorney(s) and/or agent(s) assigned to the customer number listed below, as may from time to time be amended, belonging to the firm of **Ware, Fressola, Van Der Sluys & Adolphson LLP**, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Customer Number

4955 → [ ]

Address all telephone calls to: Ware, Fressola, Van Der Sluys & Adolphson LLP at (203) 261-1234. **Address all correspondence to:**

Customer Number

4955 → [ ]

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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☐ Additional inventors are being named on separately numbered sheets attached hereto.